

- 43 -

What is claimed is:

1. An *in vivo* delivery vector comprising a plastin promoter operably linked to a gene whose induction modifies the metabolism of a cell.
2. The vector of claim 1, wherein the plastin promoter is a human plastin
5 promoter.
3. The vector of claim 1, wherein the plastin promoter comprises at least one transcriptional control element selected from the group consisting of a progesterone-responsive element and estrogen-responsive element.
4. The vector of claim 1, wherein the upstream region comprises a nucleotide
10 sequence extending from about -2265 of the 5' region of the L-plastin promoter to about the transcriptional initiation site of the L-plastin gene or fragments thereof.
5. The vector of claim 1, wherein the vector is replication deficient.
6. The vector of claim 1, wherein the vector is conditionally replication competent.
- 15 7. The vector of claim 6, wherein the vector conditionally replicates within neoplastic cells.
8. The vector of claim 7, wherein the vector does not replicate within normal epithelial cells.
9. The vector of claim 8, wherein the vector comprises the E1 adenovirus
20 gene.
10. The vector of any one of claims 1-9, wherein the vector is an adenovirus vector.



- 44 -

11. The vector of claim 10, wherein the gene encodes a molecule that metabolizes or activates a prodrug.

12. The vector of claim 11, wherein the gene is selected from the group consisting of a thymidine kinase, cytosine deaminase, a purine nucleotide phosphorylase, a
5 nitroreductase, β -galactosidase, a cytochrome P450 reductase, a deoxycytidine kinase, a carboxylesterase and a thymidine phosphorylase.

13. The vector of claim 12, wherein the vector additionally comprises a gene encoding an OPRTase.

14. The vector of claim 12, wherein the thymidine kinase is the herpes simplex
10 or varicella zoster virus thymidine kinase.

15. The vector of claim 12, wherein the purine nucleotide phosphorylase is an *E. coli* purine nucleotide phosphorylase.

16. The vector of claim 12, wherein the nitroreductase is an *E. coli* nitroreductase.

17. The vector of claim 12, wherein the cytochrome P450 is a rat or human
15 cytochrome P450.

18. The vector of claim 12, wherein the deoxycytidine kinase is a human deoxycytidine kinase.

19. The vector of claim 12, wherein the a thymidine phosphorylase is a human
20 a thymidine phosphorylase.

20. A method of sensitizing tumor cells to a chemotherapeutic agent, comprising the step of:

- 45 -

(a) infecting at least a fraction of the tumor cells with a vector of claim 11.

21. The method of claim 20, further comprising the step of:

(b) administering a prodrug.

22. A method of removing cancer cells from bone marrow or peripheral blood
5 mononuclear cells comprising the step of:

(a) infecting at least a fraction of the tumor cells with a vector of claim 11.

23. The method of claim 22, further comprising the step of:

(b) administering a prodrug.

24. The method of claim 22, wherein the bone marrow or peripheral blood
10 mononuclear cells are autologous.

P692 25. The method of any one of claims 20-24, wherein the gene is selected from
the group consisting of a thymidine kinase, cytosine deaminase, a purine nucleotide
phosphorylase, a nitroreductase, β -galactosidase, a cytochrome P450 reductase, a
carboxylesterase, a deoxycytidine kinase and a thymidine phosphorylase.

15 26. The method of either of claims 21 or 23, wherein the prodrug is selected
from the group consisting of 6-methoxypurine arabinonucleoside, acyclovir, ganciclovir
and 1-(2'-deoxy-2'-fluoro- β -D-arabinofuranosyl)-5-iodouracil, 6-methylpurine-2'-
deoxyribonucleotide, 5-fluorocytosine, a dinitrobenzamide mustard derivative,
cyclophosphamide, ifosfamide, 1- β -D-arabinofuranosylcytosine, irinotecan, and 5'-deoxy-
20 5-fluorouridine.

27. The method of either of claims 21 or 23, wherein the gene is cytosine
deaminase and the prodrug is 5-fluorocytosine.

- 46 -

File *cu3* →

28. The method of any one of claims 20-24, wherein at least about 5% of the cells are infected.
29. A recombinant adenovirus comprising the vector of any one of claims 1-9.
30. A pharmaceutical composition comprising an adenovirus of claim 29 in a
5 pharmaceutically acceptable carrier.